R E M A R K S

Priority Claim Under 35 USC 119

Item no. 5 at the bottom of page 2 of the August 20, 2008 Office Action indicated receipt of the English-language translations of applicant's priority documents. however, item no. 12 on page 1 of each of the February 19, 2008, August 20, 2008 and April 29, 2009 Office Actions did not have any indication regarding applicant's claim for priority under 35 USC 112 or receipt of the certified copies of the priority documents.

The Examiner is respectfully requested to acknowledge applicant's claim for priority under 35 USC 119 and receipt of the certified copies of the priority documents, which were received by the USPTO (see the NOTICE OF ACCEPTANCE OF APPLICATION UNDER 35 U.S.C. 371 AND 37 CFR 1.495 dated October 10, 2006).

Claim Amendments

The amendment to claims 1 to 4 to insert the terminology "for a primer" after the term "oligonucleotide" is supported in the last paragraph on page 6 of the specification.

Claims 1 to 4 and 12 to 17 were amended to include the feature of claim 5.

Minor editorial revisions were made to claim 14, item (a) and claim 33.

Rejections Under 37 CFR 1.112, First Paragraph
(Alleged Lack of "Written Description")

Claims 1 to 4 and 12 to 17 were rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement for the reasons set forth in item no. 8 on pages 4 to 6 of the Office Action.

Claims 23, 29, 35 and 41 were rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement for the reasons set forth in item no. 9 on pages 6 to 8 of the Office Action.

Claims 24, 30, 36 and 42 were rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement for the reasons set forth in item no. 10 on pages 8 to 10 of the Office Action.

Claims 25, 29, 37 and 43 were rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement for the reasons set forth in item no. 11 on pages 11 to 13 of the Office Action.

Claims 26, 32 and 38 were rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement for the reasons set forth in item no. 12 on pages 13 to 15 of the Office Action.

Claims 5, 18 to 22, 27, 28, 31, 33, 39, 40 and 52 to 54 were not included in any of the above 35 USC 112, first paragraph rejections.

As discussed above, claims 1 to 4 and 12 to 17 were amended to include the features of claim 5. Accordingly, withdrawal of each of the 35 USC 112, first paragraph rejections is respectfully requested.

Obviousness Rejections Under 35 USC 103

Claims 1 to 5, 23, 29 and 41 were rejected under 35 USC 103 as being unpatentable over Morita et al., Bioorganic & Medicinal

Chemistry letters, 12, (2002), 73-76; Braasch et al., Chemistry & Biology, 8, (2001), 1-7 and Orum et al., Clinical Chemistry, 45:11, 1898-1905, (1999) for the reasons indicated in item no. 14 on pages 15 to 23 of the Office Action.

Regarding claims 1, 2, 5, 23 and 29, it was admitted in the Office Action that Morita et al. do not specifically teach an ENA unit at the third position from the 3'-end; do not specifically teach the "intended use" of nucleotides complementary to a gene which is a target, a target gene; and do not specifically teach a mutant nucleotide.

It was admitted in the Office Action that Braasch et al. and Orum et al. do not specifically teach ENA units. It was also admitted in the Office Action that Braasch et al. and Orum et al. do not specifically teach a 2'-O,4'-C-ethylene nucleotide (ENA) unit, and do not specifically teach all of the limitations and intended uses of the claimed oligonucleotide in a single oligonucleotide.

Claims 12 to 19 and 52 to 54 were rejected under 35 USC 103 as being unpatentable over Morita et al., Bioorganic & Medicinal Chemistry letters, 12, (2002), 73-76; Braasch et al., Chemistry & Biology, 8, (2001), 1-7; Orum et al., Clinical Chemistry, 45:11, 1898-1905, (1999); and Weston et al. (USP 6,391,593) for the

reasons indicated in item no. 15 on pages 21 to 30 of the Office Action.

Regarding claims 12 to 18, it was admitted in the Office Action that Morita et al. do not specifically teach an ENA unit at the third position from the 3'-end; do not specifically teach the intended use of nucleotides complementary to a gene which is a target, a target gene; and do not specifically teach a mutant nucleotide.

It was also admitted in the Office Action that regarding claims 12 to 18, Morita et al. do not specifically teach a kit.

Claims 20 to 22, 24 to 28, 30 to 40 and 42 to 43 were rejected under 35 USC 103 as being unpatentable over Morita et al., Bioorganic & Medicinal Chemistry letters, 12, (2002), 73-76; Braasch et al., Chemistry & Biology, 8, (2001), 1-7; Orum et al., Clinical Chemistry, 45:11, 1898-1905, (1999); and further in view of Stanton, Jr. et al. (US 2001/0034023) for the reasons indicated in item no. 16 on page 31 of the Office Action.

It was admitted in the Office Action that Morita et al., Braasch et al. and Orum et al. do not teach the limitations of claims 20 to 22, 24 to 28, 30 to 40, 42 and 43.

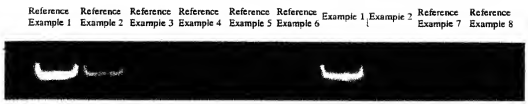
The presently claimed invention relates to an oligonucleotide having an ENA unit at the third nucleotide from

the 3'-end. An oligonucleotide having an ENA unit at the second C.nucleotide from the 3'-end does not provide the same advantageous results as an ENA unit at the third nucleotide from the 3'-end as recited in applicant's claims. In this regard, see the following portion of page 8 of the present specification:

> "The results are shown in Figure 5. When a compound, **wherein an ENA unit had been introduced into the third position from the 3'-end thereof, was used as a forward primer, in the case of the compound of Example 1, amplification of the gene of interest (216 bp) could be confirmed**, but in the case of the compound of Example 2, amplification of the gene of interest (216 bp) could not be confirmed. In contrast, when the compounds of Reference Examples 1 and 2, which were natural oligonucleotides, were used as forward primers, not only in the case of the compound of Reference Example 1, but also in the case of the compound of Reference Example 2, amplification of the gene of interest was confirmed, and thus amplification of the gene due to non-complementary binding took place. On the other hand, in the case of the compounds of Reference Examples 3 and 4, wherein an ENA unit has been introduced into the 3'-end thereof, and in the case of the compounds of Reference Examples 5 and 6, wherein **such ENA unit had been introduced into the second position from the 3'-end thereof, amplification of a gene of interest was not confirmed. These results revealed that when a compound, wherein an ENA unit has been introduced into the third position from the 3'-end thereof, is used as a primer, there is almost no non-complementary binding, thereby selectively amplifying the gene (216 bp)**." (emphasis supplied)

Fig. 5 of the present specification is reproduced as follows:

Figure 5



It is respectfully submitted that the above showing rebuts the last paragraph on page 20 of the Office Action.

It was stated in the Office Action that Morita et al. teach oligonucleotides comprising a 2'-O,4'-C-ethylene nucleotide (ENA), which is the second nucleotide from the 3'-end of the oligonucleotide. As shown above, an oligonucleotide having an ENA at the second position from the 3'-end does not provide the advantageous results as an oligonucleotide having an ENA at the third position at the 3'-end, as recited in applicant's present claims.

Morita et al. disclose the nuclease-resistance of ENA, and do not disclose any primers that are recognized by DNA polymerase, as in the presently claimed invention.

Thus, it is respectfully submitted that Morita et al. is completely different from the presently claimed invention.

As discussed above, it was admitted in the Office Action that Braasch et al. and Orum et al. do not teach a 2'-O,4'-C-ethylene nucleotide (ENA) unit.

As discussed above, it was admitted in the Office Action that Braasch et al. and Orum et al. do not teach an ENA unit.

Braasch et al. disclose many kinds of oligonucleotides having an LNA at various positions and do not particularly specify the position of the LNA. In addition, the oligonucleotide is made for detecting the Tm value, and not for detecting SNPs (single nucleotide polymorphisms).

There is no specific teaching in Braasch et al. concerning inserting a LNA (let alone an ENA) at the third position from the 3'-end of an oligonucleotide.

Orum et al. show the thermostability of octamer oligonucleotides (Table 1). The length of these oligonucleotides are different from the presently claimed invention.

Braasch et al. and Orum et al. do not teach a nucleotide length (i.e., how many nucleotides are in the oligonucleotide?) of the oligonucleotide and where and how many LNAs should be inserted in the oligonucleotide to obtain a oligonucleotide which can detect SNPs.

It is therefore respectfully submitted that Braasch et al. and Orum et al. are completely different from the presently claimed invention.

The following position was taken at the middle of page 30 of the Office Action:

> "Weston et al. teach kits comprising oligonucleotides with LNA units, DNA polymerases and PCR buffers (see column 7, lines 41 to 51, and see claims 20 and 21)."

Weston et al. do not specify the position and number of LNA units in their probes. In contrast thereto, applicant's claims specify the position (the third position) and number (one) of an ENA unit (the third nucleotide from the 3'-end thereof is a 2'-,4'-ethylene nucleotide (ENA) unit, wherein the nucleotide at the 3'-end is defined as the first nucleotide).

In addition, Weston et al. disclose a kit which comprises a following pair of probes:

(a) first probe: comprising a portion complementary to the sequence of interest and capable of hybridizing thereto, and a portion non-complementary to the sequence of interest;

(b) second probe: comprising a portion complementary to the sequence of interest and capable of hybridizing thereto, and a portion non-complementary to the sequence of interest, but complementary to that portion of the first probe which is non-complementary to the sequence of interest.

The structure of said pair of probes in Weston et al. is completely different from applicant's claims. It is therefore respectfully submitted that Weston et al. do not teach or suggest applicant's claimed kits.

The following position was taken at the middle of page 31 of the Office Action:

> "Stanton, Jr. et al. teach oligonucleotide/primers for detecting drug metabolizing."

Stanton, Jr. et al. do not teach or suggest an oligonucleotide as recited in applicant's claims (the third

nucleotide from the 3'-end thereof is a 2'-O,4'-ethylene nucleotide (ENA) unit, wherein the nucleotide at the 3'-end is defined as the first nucleotide) for detecting drug metabolizing genes.

Stanton, Jr. et al. do not disclose a method for identifying SNPs by using the oligonucleotides, as recited in applicant's presently claimed invention.

It is therefore respectfully submitted that a person having ordinary skill in the art would not consider to combine the references in the manner set forth in the Office Action.

Even assuming *arguendo* that the references are combinable, it is respectfully submitted that one of ordinary skill in the art would not arrive at applicant's present claims in view of the disclosure of the references.

Withdrawal of each of the obviousness rejections is thus respectfully requested.

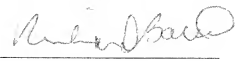
Rejoinder

If the claims of elected Group I are allowed, rejoinder and allowance of the withdrawn claims of non-elected Group II are respectfully requested (see item no. 3 on pages 4 to 5 of the November 5, 2007 Office Action).

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



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